REMARKS

Claims 14, 18, and 21 have been amended to include the term hydrophobic before active principle. Support for this amendment can be found throughout the application. For example, the paragraph bridging pages 10 and 11 of the application (paragraph [0067] of the published application). Claim 14 has also been amended to make the claimed subject matter more clear. No new matter has been added.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 14 was again rejected under 35 U.S.C. § 112, first paragraph, as being enabling for a statin as a water insoluble active, but not enabling for any active principle.

Applicants have amended claim 14 to include the term "hydrophobic" before active principle. Applicants respectfully point out that the invention as presently claimed is particularly well suited to use with hydrophobic active principles. This is demonstrated by the comparison of figures 3 and figure 4. Figure 4, using a composition within the scope of claim 14 can be seen to have a much larger etched area than that of figure 3. This represents a much larger amount of micro-emulsion present in the composition and a concomitant increased capacity to facilitate the dissolution of hydrophobic active principles in the presence of high proportions of water. This is illustrated specifically in the specification for simvastatin, a hydrophobic active principle, and the properties of the properties of the self micro-emulsifying carriers taught by the application can enable the dissolution of any hydrophobic active principle. Applicants respectfully submit that the application is enabling for all hydrophobic active principles and that the amendment entered herein has overcome this rejection. Reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. § 103(a)

Claims 14-17, 24-25, and 27 were again rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent No. 6,054,136 to Farah et al. (hereinafter "Farah"). The

Examiner contends that it would have been obvious to a person skilled in the art to use a surfactant or a co-surfactant that is a caprylic or capric ester of propylene glycol, given the lauric ester of propylene glycol and caprylic and capric fatty acid teachings by Farah.

Applicants respectfully point out that where Farah is describing caprylic and capric fatty acids it is in the context of C_8-C_{18} fatty acid esters that are not present in the surfactant or co-surfactant phase of the SMEDDS® but in the lipophilic phase. There is no suggestion in Farah to include propylene glycol monocaprylate in the co-surfactant phase of a self micro-emulsifying carrier.

The Examiner also contends that one with ordinary skill in the art would find it obvious from the teaching of Farah that fatty acid esters of propylene glycol, more specifically the caprylic and capric acid esters of propylene glycol can be used as a co-surfactant.

Again, it is respectfully submitted that there is no suggestion in Farah to use caprylic and capric acid esters of propylene glycol in the co-surfactant phase of a self micro-emulsifying carrier. Where caprylic and capric fatty acids are disclosed in Farah they are esterified with glycerol and **polyethylene** glycol, **not propylene** glycol as in the co-surfactant phase of the claimed invention. In Farah, caprylic acid and capric acids are used as part of a mixture useful in the lipophilic phase. The pending claims recite propylene glycol monocaprylate in the **co-surfactant phase** of a self micro-emulsifying carrier. This is not taught or suggested by Farah.

The Examiner further contends that using a co-surfactant that is a caprylic or capric ester of propylene glycol would be obvious in view of the lauric ester of propylene glycol and caprylic and capric fatty acid teachings by Farah. Applicant has already distinguished Farah's use of caprylic and capric fatty acid from that of the claimed invention as being localized within different phases of the self micro-emulsifying carrier. Morever, a comparison between figure 3 and 4 shows a dramatic change in the area of the microemulsion in these ternary diagrams that results from the use of propylene glycol monocaprylate in the co-surfactant phase of a self micro-emulsifying carrier (figure 4) as compared with the use of lauric esters of propylene glycol in the co-surfactant phase of a self micro-emulsifying carrier in Farah (figure 3). One skilled in the art would have no

reason to expect such a significant change in the properties of the composition on going from a lauric ester of propylene glycol to a caprylic ester of propylene glycol in the co-surfactant phase of a self micro-emulsifying carrier. This dramatic and unexpected increase in the percentage of the solution that is a micro-emulsion provides for the unexpected increase in the rate of dissolution of hydrophobic active principles achieved by the presently claimed invention.

On page 4 of the office action, the Examiner contends that Farah teaches the use of caprylic and capric fatty acids in the surfactant composition and provides enhanced solubility and bioavailability of the active ingredient. The Examiner further contends that this advantage taught by Farah would make the results of increased dissolution of the active principle an expected result.

Applicants disagree. The caprylic and capric fatty acids in Farah are estererified with a glycerol and polyethylene glycol, not propylene glycol and are not present in the co-surfactant phase of a self micro-emulsifying carrier. It would not have been obvious to a person skilled in the art that the use of propylene glycol monocaprylate in the co-surfactant phase of a self micro-emulsifying carrier would provide pharmaceutical compositions that dramatically increase the dissolution of hydrophobic active principle. A person skilled in the art would not have been motivated to substitute a propylene glycol monocaprylate for the lauric esters of propylene glycol disclosed in Farah in the co-surfactant phase of a self micro-emulsifying carrier since there would have been no reasonable expectation of success with respect to the increased area of the microemulsion and concomitant increase in the dissolution of hydrophobic active principles.

A recent Federal Circuit case, citing KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 167 L.Ed.2d 705 (2007), notes that "the Court [in KSR] acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir 2007) p. 1356-1357. Here, the Examiner has not identified any reason why a person skilled in the art would substitute a caprylic ester of propylene

glycol (propylene glycol monocaprylate) in the co-surfactant phase for the lauric esters of propylene glycol used in Farah.

Again, on reviewing the table in Example 4, on comparing formula 1 (results shown in Fig 3) and formula 2 (results shown in Fig 4), Applicants respectfully point out that a dramatic and unexpected increase in the area of the microemulsion on going from a lauric ester of propylene glycol in the co-surfactant phase of a self micro-emulsifying carrier to a caprylic ester of propylene glycol (propylene glycol monocaprylate) in the co-surfactant phase of a self micro-emulsifying carrier is obtained. It is respectfully submitted that since these results are unexpected and that there would have been no reason for a person skilled in the art on reading Farah to substitute a caprylic ester of propylene glycol (propylene glycol monocaprylate) in the co-surfactant phase of a self micro-emulsifying carrier for the lauric esters of propylene glycol used in Farah that all of the claims are patentable over Farah. Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 18-23 were again rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent No. 6,054,136 to Farah et al. (hereinafter "Farah") in view of Lipari et al (International Publication No. WO 00/37057) hereinafter "Lipari").

The Examiner contends that a person of ordinary skill in the art would find it obvious to use propylene glycol monocaprylate in view of the disclosure in Lipari of propylene glycol mono and di-caprylate along with disclosure in Farah that caprylic and capric acid esters of propylene glycol can be used as co-surfactants. Applicants, once again, point out that there is no suggestion in Farah to use propylene glycol monocaprylate in the co-surfactant phase. Moreover, while page 5 of Lipari, pointed to by the Examiner, mentions propylene glycol dicaprylate/dicaprate, there is no teaching of a self micro-emulsifying carrier as in the claimed invention. In order to make out a prima facie case of obviousness there must be a reason or motivation to combine references. Lipari does not relate to self micro-emulsifying carriers and there would be no reason for a person skilled in the art to take the mere mention of an ingredient from a composition identified as a "lipid regulating agent" as a suggestion to include such a component in the co-surfactant phase of the self micro-emulsifying carriers recited in the claims. The examiner, for

reasons unclear to the Applicants, states that "the teaching of Farah... that fatty acid esters of propylene glycol, more specifically, the caprylic and capric acid esters of propylene glycol can be used as co-surfactant" would make this combination obvious. Applicants again respectfully submit that the Examiner has not shown where in Farah caprylic and capric acid esters of propylene glycol are disclosed as being present in the co-surfactant phase of a self micro-emulsifying carrier. Applicants respectfully submit for the foregoing reasons that Farah and Lipari either combined or separately do not teach or suggest the claimed invention and respectfully request reconsideration and withdrawal of this rejection.

Claims 26 and 28 were again rejected under 35 U.S.C. § 103 as being unpatentable over Farah in view of Lipari and further in view of U.S. Patent No. 6,248,363 to Patel et al. (hereinafter "Patel"). Applicants note that the Examiner has indicated claims 18-23 in this rejection but understand that the Examiner is referring to claims 26 and 28 in this rejection.

The Examiner cites to various portions of Patel that disclose lauric macrogolglycerides as a surfactant, and points to disclosure relating to the reaction of alcohol's such as propylene with natural and or hydrogenated oils to form surfactants and that a preferred alcohol is propylene glycol. The Examiner then combines this disclosure with Farah and Lipari. Applicants emphasize again that nothing in Farah or Lipari teaches or suggests using propylene glycol monocaprylate in the co-surfactant phase of a self micro-emulsifying carrier. Patel, discloses a solid pharmaceutical composition having a substrate and an encapsulation coat. Moreover, the compositions disclosed in Patel are directed to the solubilizing **hydrophilic** pharmaceutical active ingredients whereas the present claims are directed to **hydrophobic** active principles. The examiner is reminded that for a prima facie case of obviousness, the prior art must teach or suggest all of the claim limitations and none of these references either alone or in combination teach the use of propylene glycol monocaprylate in the co-surfactant phase of a self micro-emulsifying carrier. Applicants respectfully request reconsideration and withdrawal of this rejection.

Since there are no other outstanding issues, the application is believed to be in condition for allowance. Reconsideration and allowance of the application are therefore respectfully requested.

If the Examiner has any questions, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

If any additional fees are due, or an overpayment has been made, the Commissioner is authorized to charge, or credit, U.S. Deposit Account No. 08-1935 for such sum.

Respectfully submitted,

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